would resume payment in 1997, but only for a limited number of patients participating in a seven-year study to be conducted by the National Institutes of Health.

HCFA's announcement stirred up strong sentiments among medical professionals accustomed to hashing out the pros and cons of new procedures among themselves. Many agree on the need for further research. Others, however, dismiss the study as a political move to cut costs. Lung reduction surgery costs between \$35,000 and \$70,000.

Although often considered new, LVRS dates back to the late 1950s, when University of Maryland surgeon Otto Brantigan performed the surgery on 33 patients. Brantigan theorized that emphysema patients would breathe more easily with smaller lungs. An emphysematous lung expands as the disease breaks down the walls in the spongy organ's air sacs. Pressure from the distended lungs prevents the diaphragm from pushing air out effectively. By reducing the lungs' size, Brantigan believed he could improve the mechanics of the breathing muscles. Unfortunately, he had no means of measuring his patients' improvement. His procedure was largely forgotten until its recent revival, led by Cooper at Barnes Hospital in St. Louis.

Cooper typically splits his patients' sternums and uses a scalpel to remove 20–30% of each lung. His first 20 patients demonstrated a remarkable 82% increase in their forced expiratory volume, the amount of air they can blow out. Seventy-one percent were able to give up supplemental oxygen. Other surgeons report substantial improvements in at least two-thirds of their LVRS patients. "Our patients feel dramatically better and breathe better," said John Chen, assistant chief of cardiothoracic surgery at the University of California–Irvine Medical Center.

But what about the minority of patients who fail to improve, and the 5-10% who die? Will patients who have had the surgery live any longer than those receiving traditional treatment with drugs and rehabilitation? These are among the questions NIH officials expect their study to answer. The NIH's National Heart, Lung and Blood Institute will manage the study, which is slated to begin in 1997. Approximately 15 medical centers will be chosen to conduct clinical trials. Approximately 3,000 patients will participate. All will receive intensive pulmonary rehabilitation and drug therapy. Half, chosen at random, then will undergo LVRS. Researchers will compare the progress of the two groups.

Those who support the study point out the need for more data. "We should know up front who improves and who does not," said Jonathon Truwit, interim division chief of pulmonary and critical care medicine at the University of Virginia in Charlottesville. "If we're setting these patients' clocks back, let's find out how far back."

Pulmonologist and ethicist Mark Tonelli of the University of Washington in Seattle pointed out the government's success in regulating the pharmaceutical industry. "If this were a new drug, instead of a new type of surgery, the Food and Drug Administration would require extensive testing," he said. "I think the study is a good model."

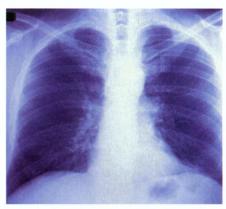
Critics object to the random selection that will deny surgery to half the candidates. They say drugs and rehabilitation have never produced the dramatic improvements seen in some LVRS patients. "We see this as a government ploy to hold back expenses," said Rodney Landreneau, head of thoracic surgery at Allegheny General Hospital in Pittsburgh.

HCFA's Sheingold countered, "We do not base our decisions on cost. We base our decisions on effectiveness. However, we're all forced to assure the highest quality of care while containing costs." Sheingold added that the LVRS study may be just a hint of future government oversight of surgical procedures. "HCFA and the NIH are looking into studying other areas, including kidney/pancreas transplants," he said. "This is a long overdue marriage of the payment agency and the best scientific agency to provide data about what works in health care."

Promising Lung Cancer Vaccine

An antibody developed by researchers at Memorial Sloan-Kettering Cancer Center (MSKCC) appears to prolong the lives of patients with small cell lung cancer. Patients who received injections containing the antibody BEC2 and Mycobacterium bovis, a strain of bacteria that stimulates the immune system, were found to live longer than patients who received only the standard treatment for small cell lung cancer, which is chemotherapy with or without radiation. Small cell lung cancer is usually fatal, with a 15-20% long-term survival rate for patients in whom the cancer is contained to the chest, and only a 0-5% long-term survival rate for those in whom the cancer has spread beyond the chest. The current median survival period, for patients diagnosed with small cell lung cancer, is 7–14 months.

To create BEC2, the researchers emulated the structure of GD3 ganglioside, a nonprotein molecule found in certain can-



A shot in the lungs. A new antibody may help patients with small cell lung cancer live longer.

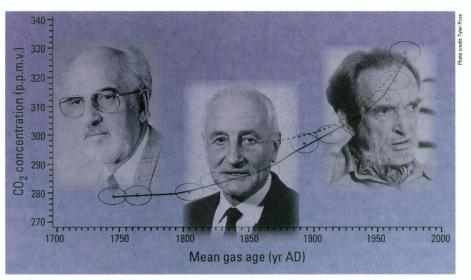
cer cells, such as small cell lung and melanoma. GD3 is not recognized by the body as a foreign molecule and therefore does not usually trigger an immune response, says Stefan Grant, an attending physician at MSKCC and co-principal investigator of the project to develop the antibody. The researchers found that BEC2 is recognized as foreign and, because their structures are similar, stimulates the production of antibodies against both BEC2 and GD3. The antibodies signal the immune system to destroy the cells containing GD3 and BEC2, thus eliminating the cancer.

MSKCC researchers conducted a clinical trial on eight patients with small cell lung cancer who had received chemotherapy. The researchers administered the vaccine to the participants five times during a period of 10 weeks. Six of the participants completed the immunizations and were evaluated, and four of these were found to be free of the cancer and healthy three years after their diagnoses.

The control group for this study consisted of 34 patients who had received similar chemotherapy at MSKCC. The median survival for this group was 16.2 months, whereas the median survival for the group treated with BEC2 was more than 36 months. The study was presented at the American Society of Clinical Oncology annual meeting in May in Philadelphia.

The only side effect seen thus far is a local reaction at the site of the injections, which is manifested by inflammation and leaves a scar, said Grant. MSKCC researchers are now planning a larger study to test the vaccine. "We are planning a large randomized phase-3 trial, which we anticipate [to be conducted] towards the middle of next year," Grant said. The study will involve more patients and a larger control group.

Although the vaccine has not yet been thoroughly tested, MSKCC researchers are



The Icemen cometh. (I. to r.) Hans Oeschger, Claude Lorius, and Willi Dansgaard were awarded the 1996 Tyler Prize for their documentation of climate change through analysis of ice.

Graph source: Neftel A, Moor E, Oeschger H, Stauffer B. Evidence from polar ice cores for the increase in atmospheric CO₂ in the past two

Graph source: Neftel A, Moor E, Oeschger H, Stauffer B. Evidence from polar ice cores for the increase in atmospheric CO₂ in the past tw centuries. Nature 315(May 2):45–46 (1985). MacMillan Magazines Ltd.

optimistic. "I do feel positive, but we acknowledge that these results are preliminary," Grant said. "We consider the results extremely encouraging, but as enthusiastic as we are, we all agree that we have not proven [the vaccine's efficacy]." Grant said that from a scientific standpoint, "only a rigorously controlled trial" can prove the effectiveness of the vaccine.

The researchers are also hoping to use the vaccine to treat melanoma. Preliminary tests on patients with melanoma, led by Paul Chapman of the clinical immunology service at MSKCC, have been promising, and a phase-3 trial is being planned, Grant said.

Climate Change Researchers Capture Tyler Prize

Three scientists whose work has documented more than 150,000 years of global climate change through the collection and analysis of glacier and polar ice have been awarded the 1996 Tyler Prize for Environmental Achievement. Willi Dansgaard of the University of Copenhagen, Claude Lorius of the French Institute of Polar Research and Technology, and Hans Oeschger of the University of Bern shared a cash prize of \$150,000 and received gold medallions at an awards dinner in Los Angeles.

Preserved within the great polar ice caps is a remarkable record of the earth's climate extending back hundreds of thousands of years. Encased within the caps are carbon dioxide and other gases, the dust of numerous volcanic eruptions, evidence of fierce global storms, and other traces of cli-

mate change deposited during the span of human existence.

"The composition of the ice itself tells us about the temperature and atmospheric conditions at the time the ice was formed," said Dansgaard. "So going deep into the ice is like sticking a thermometer backwards in time." Searching for clues to the earth's climatic history through the study of ancient ice was a revolutionary idea when first proposed in the 1950s. Today, it is the foundation of global climate research. "Data from this work is used in virtually all scientific studies and reports about global warming to emphasize the potential of atmospheric pollution to adversely affect climate," said Robert P. Sullivan, chair of the Tyler Prize Executive Committee, which annually selects the prize winners.

The first polar deep ice core drilling field expedition took place in 1966 in Greenland. Since that time, additional samples have been retrieved from Norway and Antarctica. Drilling, involving international teams of scientists, takes place under some of the most extreme weather conditions on earth. The cores are less than 4 inches in diameter and can measure more than a mile in length.

Once removed from the field, it often takes decades of laboratory analysis to unlock the oxygen isotopes and other traces of ancient atmospheres trapped for millennia in the ice. The result of the researchers' painstaking work is a detailed look back in time. Of particular interest to environmental scientists has been the reconstruction of atmospheric carbon dioxide and methane levels during the last 300

years, which shows a strong relationship between global climate and the chemical composition of the atmosphere. This data provides the most dramatic and convincing evidence of global warming tied to human activities.

The Tyler Prize was established in 1973 by Los Angeles philanthropists John and Alice Tyler as an international award honoring significant scientific achievements in all disciplines of environmental research and environmental protection. Through their work, Tyler laureates have focused worldwide attention on environmental problems and motivated effective action toward solutions. Three past Tyler Prize winners have subsequently been awarded the Nobel Prize in Chemistry.

The 11-member Tyler Prize Executive Committee comprises esteemed environmental scientists, several of whom are past Tyler Prize recipients. The Tyler Prize is administered by the University of Southern California.

Assessing Free Radical Damage

Free radicals have developed a bad reputation, in the scientific and popular press but recent research shows how difficult a causal relationship between free radicals and disease may be to prove. Free radicals are unstable oxygen molecules that can interact with proteins, carbohydrates, lipids, and DNA, and thereby can have diverse effects on cellular function. Although some evidence points in the direction of free radicals as a culprit in a multitude of diseases, including cancer, cardiovascular disease, and Alzheimer's disease, a direct causal relationship in human beings has yet to be established. A primary reason for this is that the generation of free radicals in human beings has been difficult to measure. Free radical damage has been statistically inferred, measured by in vitro testing, and implicated in autopsy results, but never established in living humans. This has also made it "difficult to identify drugs or vitamins that may act as antioxidants to combat the effect of free radicals, and therefore, to identify appropriate doses which could be assessed in clinical trials," says Garret FitzGerald, chairman of the department of pharmacology and a professor of cardiovascular medicine at the University of Pennsylvania Medical Center, Philadelphia.

However, in a recent study, FitzGerald and his colleagues were able to noninvasively measure the effects of free radicals on the human body. The study was reported in the 1 July 1996 issue of *Circulation*, a journal of the American Heart Association.